**Research Projects and Clinical Trials: our role**

From time to time Nerve Tumours UK is approached with requests to support researchers working in the field of neurofibromatosis either financially or by letting our members know about research that is taking place and inviting them to take part. The kind of research project varies but can include:

- Clinical studies where a team of health professionals want to study one aspect of neurofibromatosis (NF) in detail
- Psychosocial studies where health professionals or social scientists want to look at how NF affects people and the way they live their lives
- Clinical trials where a clinical team are studying a new treatment or the use of particular investigations in the different forms of NF.

Most people are unfamiliar with the process of research and clinical trials, so we offer here some general information about how clinical trials work and how Nerve Tumours UK deals with requests for support from researchers.

## The starting point of all research - ethical approval

In years gone by doctors could just decide to try out a treatment for something without consulting anyone. This resulted in problems not only for patients who often were not aware they were being used as "guinea pigs", but also the treatments that initially appeared to work, were then used by other doctors, and only later found to cause harm. Fortunately this has all changed! All research involving human subjects (and animals too) is tightly regulated and has to be reviewed by an independent ethics committee before starting. In the case of studies with drugs, it is also necessary to obtain approval from national drug regulatory agencies, for example the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK.

## Role of Nerve Tumours UK

If the charity is asked to support research by making a financial contribution to work being undertaken, or if we are asked to help with recruitment of patients for a particular research project, that request is automatically submitted to the chair of our Medical Advisory Board (MAB chair currently Professor Ros Ferner). We do not have the resources to evaluate the merits of any research being undertaken ourselves and so all such requests for our help are forwarded to the MAB whose members have the skills and experience individually and collectively to provide us with the appropriate guidance. This process ensures that the projects we do support are of consistent quality, and have the necessary approvals (both ethical and other) at the outset. The MAB members require full detailed information about the proposed project before their evaluation can take place.

## Why research is important

All care provided by the NHS now has to be "evidence based". This means that there needs to be research before new tests or treatments are introduced. Who does the research depends on the project: they may be hospital doctors or other health professionals such as psychologists or speech therapists. They may be from a social

science research group or be laboratory based researchers. Most researchers are based in large hospitals, research institutes, universities, or social care services. It is normal practice to explain to participants who is funding the work. Participants may also be offered information at the end of the project if they wish.

Health research covers a wide range of activities not just new drugs or a new treatment once a problem has occurred. It can encompass areas such as health prevention, the psycho-social impact of health problems, or early detection of illness by means of testing, the relationship between diet and disease, or improving the quality of life of patients. Clinical trials enable doctors and other professionals to gather evidence to identify particular problems linked to a diagnosis or to gather evidence to identify particular problems linked to a diagnosis or to gather evidence about what treatment works effectively.

## Who can take part in research?

Obviously this depends on the particular trial and the group of patients being recruited. In most trials there are some basic criteria explained at the outset which describe the focus of the trial and eligibility for inclusion. For example a specific diagnosis, a specific age range, a locality near the research centre. Some patients may be excluded because of other health factors, specific treatments they are already receiving or have received in the past, or because of other factors such as pregnancy. This is to ensure the results are as reliable and unbiased as possible.

If you decide to volunteer to be part of a study, and meet the criteria for entrance, you will be given a full detailed explanation of everything that the study entails, and asked to sign a form giving your consent. It is important to know that even if you have volunteered and signed consent, you can always withdraw from a study, at any time, without having to give a reason.

## What are clinical trials?

A clinical trial is a tool of medicine that involves people (patients) in research. The purpose of the trial may be to establish whether a treatment or medical technique is safe and effective, and whether the outcome brings positive benefits to the person taking part. The trial will usually consider whether a new treatment works better than the treatment being used currently. Trials also evaluate potential risks involved such as any adverse side effects. Trials can be used to determine treatment (drugs), to prevent illness, to screen for health problems, to diagnose a condition or to evaluate quality of life. Trials may recruit both patients and people who are in good health.

In the UK there are strict guidelines when new drugs are being considered for use in treating patients. If a drug is developed in a laboratory, before it can be used to treat patients it will be tried out in a step by step way: incremental "phases" from 0 to 3. The researchers undertaking trials involving patients will offer a treatment they believe is as effective or better than the current best available treatment. The trials follow strict rules and guidance called a protocol. There are UK and European regulatory organisations whose specific role is to ensure the safety of medicines and they are responsible for approving studies of new drugs and licensing new drugs for use in the UK.

## Phases of clinical trials

Doctors and health professionals use evidence from their work in clinical trials to understand what treatment works best for patients with a particular health problem. They may recruit patients specific to their research or people in good health. The doctors must

follow the agreed protocol to ensure safety of all participants.

The phases of trials are like the steps on a ladder and numbered 0 to 4. Broadly speaking a phase 0 trial recruits a very small number of people using a very small dose of the drug under scrutiny to work out what happens to the drug in the body. Phase 1 will focus on working out if a treatment is safe and what the dose is likely to be. Phase 2 considers how well a treatment works. At this stage the trials are often "randomised". In other words the patients are assigned to a group taking the new drug or to a group taking a placebo or comparator drug. Neither the trial participants nor the health professionals they meet know who is taking the new drug. This is because of what is called the "placebo effect" Often people in a trial will report feeling generally slightly better as being in the trial allows them much more frequent access to health professionals interested in their condition.

Phase 3 tests the new treatment in a much larger group of patients to be completely sure that the drug works, and is safe. Phase 3 studies may compare against the existing treatments or, if there is no treatment, the trial will be larger "placebo controlled" studies.

Phase 4 trials are conducted only after a new treatment has been licensed, and will consider the effects of prolonged use of a drug treatment on a much larger group of patients or perhaps finding new uses.

## Quality of life studies

This type of study sets out to identify ways of improving a person's sense of well-being. It usually involves completing a questionnaire. The research may focus on the psychological impact of an illness or treatment, the financial impact for a patient and their family, or the specific nature of the difficulties themselves.

## What trials does Nerve Tumours UK currently support?

At the current time we do not have sufficient income to fund large research projects ourselves but we are active in promoting research studies that our MAB has approved. Examples of this are:

- Putting people who are having NF1 related tumours removed in touch with Professor Upadhyaya's group in Cardiff. They are studying the genetic changes that occur when an internal plexiform neurofibroma becomes malignant.
- The SANTA trial in Manchester which is a phase 2 study looking at whether simvastatin reduces the symptoms of NF1 associated autistic spectrum disorder (ASD).

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